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Reappraisal of the relation between blood lead concentration and blood pressure among the general population in Taiwan

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Abstract

***Objectives*—The relation between blood lead concentration (PbB) and blood pressure was examined in a Taiwan nationwide population survey of PbB from July 1993 to June 1994.**

***Methods*—After multistage sampling procedures, 2800 subjects (1471 males and 1329 females) with a mean (range) age of 44 (15–85) years were enrolled in this study. Anthropometric, blood pressure, and lifestyle factors were measured during household visits. The PbB was measured with a flameless atomic absorption spectrophotometer and all specimens were analysed in triplicate.**

***Results*—The mean (range) PbB among all study subjects was 6.5 (0.1–69.1) µg/dl; among males it was 7.3 (0.1–69.1) µg/dl and among females 5.7 (0.1–40.1) µg/dl). The mean (range) systolic blood pressure among all subjects was 123 (80–210) mm Hg, among males it was 127 (80–200) mm Hg and among females 119 (80–210) mm Hg. The diastolic blood pressure among all subjects was 78 (40–150) mm Hg; among males it was 80 (40–130) mm Hg; and among females 75 (40–150) mm Hg. Age, body height, body weight, and body mass index (BMI) were significantly correlated with systolic blood pressure or diastolic blood pressure in both sexes. The PbB (or the natural logarithmic transformed PbB) was not significantly correlated with blood pressure among males or females. After adjustment for the potential confounders of age, age^2, BMI, milk intake, alcohol consumption, and cigarette smoking, systolic blood pressure was significantly associated with PbB among males with a regression coefficient (β) of 0.185 (p=0.015). No significant association between PbB and blood pressure was found among females.**

***Conclusions*—From this study, only a weak association between systolic blood pressure and PbB was found among males. There was no strong evidence that PbB was a good predictor of blood pressure. However, the possiblity that long term high body lead burden could cause high blood pressure could not be ruled out on the basis of this survey.**

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Lead is a dense silvery metal that can be easily cast, moulded, and extruded. It is often used to make sheeting and pipes, and its compounds are often used in the chemical industry. Environmental and occupational lead pollution is a common concern in developing and industrial countries and it is a worldwide public health problem. It has become an important issue for environmental health and occupational medicine in these countries.

Lead intoxication is involved with multiple systems, and causes neuropsychological effects, atherosclerotic disorders, metabolic bone effects, reproductive effects, nephrotoxicity, and carcinogenesis.[1,2] Several studies have shown that increased blood lead concentration (PbB) is associated with an increase in blood pressure. After adjusting for age, body mass index (BMI), and nutritional factors, PbB still correlated well with blood pressure.[3,4] A meta-analysis showed that blood pressure can be decreased by 1.25 mm Hg after the PbB is reduced from 10 µg/dl to 5 µg/dl.[3] The diastolic blood pressure was significantly associated with PbB among females and there was a significant association between changes in PbB and changes in systolic blood pressure in males. There was a positive association between mortality from coronary heart disease and PbB and the mortality from hypertension and cerebrovascular disease among workers exposed to lead was higher than that in the general population.[5,6] Workers exposed to low concentrations of lead had higher mortality from cerebrovascular disease than controls; however, this trend has declined and become insignificant in recent years.[5] Other studies have shown that there was no consistent association between mortality from cardiovascular disease and exposure to lead at work and, after controlling for other potential confounders, the association between PbB and mortality from cardiovascular disease was weak and non-significant.[8–10] Hense there is controversy between studies on exposure to lead and cardiovascular indices.

The purpose of this study was to evaluate the relation between PbB and blood pressure among the general population in Taiwan.

Material and methods

STUDY DESIGN AND SAMPLING

We conducted a multicentre cross sectional nationwide PbB survey from July 1993 to June 1994 in Taiwan. This survey was conducted by visiting households. People who were older than 15 years and had been registered as living

Table 1 General characteristics of study subjects of different sexes

Variables	*Mean*	*SD*	*Minimum*	*Maximum*
Total (n=2800)				
Age (y)	44.3	15.4	15.0	85.0
Body weight (kg)	61.6	10.7	36.0	105.0
Body height (cm)	161.6	7.9	132.0	192.0
Body mass index (kg/m^3)	23.6	3.5	15.2	39.4
SBP (mm Hg)	123.2	18.0	80.0	210.0
DBP (mm Hg)	77.8	11.4	40.0	150.0
Blood lead (μg/dl)	6.5	4.7	0.1	69.1
Male (n=1471)				
Age (y)	45.6	15.9	15.0	85.0
Body weight (kg)	66.2	10.2	40.0	105.0
Body height (cm)	166.7	6.1	137.0	192.0
Body mass index (kg/m^3)	23.8	3.3	15.5	39.4
SBP (mm Hg)	126.7	17.2	80.0	200.0
DBP (mm Hg)	80.0	11.2	40.0	130.0
Blood lead (μg/dl)	7.3	5.2	0.1	69.1
Female (n=1329)				
Age (y)	42.7	14.7	15	84
Body weight (kg)	56.6	8.8	36.0	100.0
Body height (cm)	155.9	5.4	132.0	176.0
Body mass index (kg/m^3)	23.3	3.5	15.2	38.1
SBP (mm Hg)	119.4	18.1	80.0	210.0
DBP (mm Hg)	75.4	11.2	40.0	150.0
Blood lead (μg/dl)	5.7	3.9	0.1	40.1

SBP=systolic blood pressure; DBP=diastolic blood pressure.

in Taiwan for >6 months were the eligible study population. The researchers (who had received training for this survey) visited every household that was sampled, and before the visit a postal notice and telephone call were given to ensure that the study participants would be present during the visit.[11]

After multistage procedures with sampling proportional to the population, we selected the study subjects according to the urbanisation level and the size of villages of Taiwan in 1994. We first sampled the villages. In Taiwan, there were 21.13 million people living in 367 villages in 1994. According to the level of urbanisation and industrialisation, these villages were classified into 24 strata; we randomly selected 82 villages proportional to the urbanisation levels. Secondly, we sampled the study households. The numbers of households sampled from the selected village were proportional to the population size of each village. In total, we sampled 2919 households. Finally, we randomly sampled one person from each selected household to become the study population. A replacement was permitted if the sampled subject refused or failed to respond, another member or volunteer of the same household or the next neighbourhood was substituted. There was no significant difference in general characteristics or PbB between the 1503 people originally sampled and the replacement population in this survey.[11]

Table 2 Pearson's correlation coefficients between study variables of both sexes

	BW	*HT*	*BMI*	*SBP*	*DBP*	*Lead*	*LogPb*
Male (n=1471):							
Age	−0.045	−0.298	0.103	0.417	0.242	0.007	−0.022
BW		0.419	0.872	0.186	0.217	−0.009	−0.002
HT			−0.072	−0.081	−0.015	−0.033	−0.017
BMI				0.248	0.247	0.008	0.007
SBP					0.670	0.049	0.035
DBP						0.037	0.028
Lead							0.824
Female (n=1329):							
Age	0.182	−0.301	0.318	0.492	0.331	0.051	0.013
BW		0.267	0.898	0.257	0.270	0.024	0.014
HT			−0.179	−0.094	−0.074	−0.048	−0.055
BMI				0.302	0.310	0.048	0.040
SBP					0.741	0.018	−0.001
DBP						−0.006	−0.016
Lead							0.816

BW=body weight; HT=body height; BMI=body mass index; SBP=systolic blood pressure; DBP=diastolic blood pressure; LogPb=logarithmic transformed blood lead concentration.

DATA COLLECTION

General information

General demographic information and lifestyle characteristics (including dietary pattern, cigarette smoking, and alcohol intake) were obtained with a structured questionnaire during the household visit.

Anthropometric measurements

Body weight was measured with a standard beam balance scale with the subjects standing barefoot and wearing light indoor clothing. Weight was recorded to the nearest 0.1 kg. Height was measured with a ruler attached to a scale and was recorded to the nearest 0.5 cm. We calculated BMI as the ratio of body weight to body height^2, and expressed it as kg/m^2.[12]

Blood pressure measurements

After the subjects had rested for 15 minutes, in the sitting position, blood pressure was measured in the right arm with a standard mercury sphygmomanometer. The pressures at the first and fifth phase Korotkoff sounds were recorded as systolic and diastolic blood pressure. A second blood pressure reading was taken after a 5 minute rest interval. The average of these two measurements was used in the analyses.

Blood lead measurements

Venous whole blood specimens were collected in a lead free heparinised vacutainer. The blood samples were stored at 4°C until the analyses (2 weeks at most). The PbB was measured by flameless atomic absorption spectrophotometer connected to a data processor. All specimens were analysed in triplicate, and the mean was taken (SD <7%). External and internal quality controls were applied to each series of analysis.[11] The proficiency and accuracy tests showed that the measurements were within the acceptable criteria proposed by the Quebec Center for Toxicology Inter-laboratory Comparison programme Canada, and the United States Centres for Disease Control and Prevention, and the variations of measurements between laboratories were <2 μg/dl.[11 13]

STATISTICAL METHODS

Data are expressed as the mean (SD) PbB after natural logarithmic transformation for an approximation of normal distribution. All analyses were stratified by sex to avoid any potential difference of PbB and blood pressure due to sex.

We calculated Pearson's correlation coefficients to evaluate the relation between the study variables and PbB with sex specification. Multiple regression analyses were used to evaluate the association between blood pressure and PbB after controlling for other potential confounders.[14 15] After univariate analyses, any variables with a p value <0.1 were selected as candidates for the multivariate analysis model as were all variables of known biological

Table 3 Regression analysis of blood lead and systolic blood pressure before and after adjusting for potential confounders in different sexes

Independent variables	*Regression coefficient (β)*	*Standard error of β*	*p Value*	*R^2*
Male (n=1471):				
Age*	0.450	0.026	<0.001	0.174
Body mass index	1.270	0.130	<0.001	0.061
Blood lead	0.163	0.086	0.058	0.002
Blood lead†	0.185	0.076	0.015	0.241
Female (n=1329):				
Age*	0.605	0.029	<0.001	0.242
Body mass index	1.544	0.134	<0.001	0.091
Blood lead	0.082	0.126	0.516	0.001
Blood lead†	−0.057	0.109	0.603	0.274

*Univariate regression analyses with age, body mass index, or blood lead as independent variables, and blood pressure as dependent variable.
†After adjusting for potential confounders of age, age^2, body mass index, milk intake, alcohol consumption, and cigarette smoking with model R^2.

Table 4 Regression analysis of blood lead concentration and diastolic blood pressure before and after adjusting for potential confounders in different sexes

Independent variables	*Regression coefficient (β)*	*Standard error of β*	*p Value*	*R^2*
Male (n=1471):				
Age*	0.171	0.018	<0.001	0.059
Body mass index	0.824	0.084	<0.001	0.061
Blood lead	0.079	0.056	0.157	0.001
Blood lead†	0.075	0.053	0.159	0.117
Female (n=1329):				
Age*	0.253	0.020	<0.001	0.109
Body mass index	0.984	0.083	<0.001	0.096
Blood lead	−0.017	0.078	0.833	0.001
Blood lead†	−0.083	0.072	0.250	0.171

*Univariate regression analyses with age, body mass index, or blood lead as independent variables and blood pressure as dependent variable.
†After adjusting for potential confounders of age, age^2, body mass index, milk intake, alcohol consumption and cigarette smoking with model R^2.

importance for blood pressure. We used a backward elimination procedure to select the variables for the final model. The final model included those variables still significant at the $p<0.05$ level and with biological relevance in predicting blood pressure. Variables that did not contribute to the model based on the selection criteria were eliminated and a final model was fitted. For the final model, the independent variables comprised continuous variables such as age, age^2, BMI, and PbB, and categorical variables such as milk intake, alcohol consumption, cigarette smoking, PbB, and systolic or diastolic blood pressure were the dependent variables. Age^2 was included as a non-linear term.

The study subjects, stratified by sex, were divided into three subgroups by PbB: <10, 10-20, and >20 µg/dl, and the mean blood pressures were compared by analysis of variance (ANOVA) after adjustment for age, age^2, BMI, milk intake, alcohol consumption, and cigarette smoking.[15]

Table 5 Adjusted blood pressure among different blood lead groups with sex stratification*

Blood lead	*<10 µg/dl*	*10–20 µg/dl*	*>20 µg/dl*
Male (n)	1213	218	40
SBP (mm Hg)	126.1 (16.9)	129.1 (18.7)	129.1 (17.1)
DBP (mm Hg)	79.7 (10.8)	81.4 (12.9)	80.1 (11.9)
Female	(n=1206)	(n=105)	(n=18)
SBP (mm Hg)	119.4 (18.0)	119.0 (19.8)	119.9 (16.5)
DBP (mm Hg)	75.5 (11.3)	74.4 (11.3)	74.6 (10.6)

*Mean (SD) adjusted for age, age^2, body mass index, milk intake, alcohol consumption, and cigarette smoking.
SBP=systolic blood pressure; DBP=diastolic blood pressure.

Results

We sampled 2919 people in this survey. After excluding 119 subjects who had incomplete or missing data, the final sample for analysis was 2800 subjects (1471 males and 1329 females) with a mean (range) age of 44.3 (15–85) years. The general characteristics of the study population are shown in table 1. Among all study subjects, the mean systolic blood pressure was 123 and diastolic blood pressure 78 mm Hg, and the mean (range) PbB was 6.5 (0.1–69.1) µg/dl.

Table 2 shows the Pearson correlation coefficients between age, body weight, body height, BMI, blood pressure, and PbB among males and females. In both sexes, age, body weight, and BMI were positively correlated with systolic and diastolic blood pressure. There was no significant correlation between age, body weight, BMI and PbB or the logarithmic transformed PbB among males or females. There was no significant correlation between blood pressure and PbB or the logarithmic transformed PbB in either sex.

Tables 3 and 4 present the sex specific multiple regression analyses to evaluate the association between PbB and blood pressure after adjustment for the potential confounders of age, age^2 BMI, milk intake, alcohol consumption, and cigarette smoking. The final model can explain about 25% and 15% of the total variance of systolic and diastolic blood pressure. Among males, the regression coefficients of PbB and systolic blood pressure were of borderline significance before and after adjustment for other potential confounders ($p=0.058$ and $p=0.015$ respectively). The PbB was not significantly associated with diastolic blood pressure after adjustment for other potential confounders and did not seem to be a strong predictor for diastolic blood pressure in either sex. Among females, there was a trend for increasing systolic and diastolic blood pressure when PbB was lowered. Our results also showed that PbB was not as good a predictor of blood pressure as either age or BMI among this study population.

Table 5 shows sex stratified blood pressure (after adjustment for age, age^2, BMI, milk intake, alcohol consumption, and cigarette smoking) among the subgroups with different PbB. The subgroups with higher PbB did not show higher blood pressures than the subgroups with lower PbB. There was no significant difference in blood pressure among subjects with different concentrations of PbB.

Discussion

In this study, we only found a borderline association between systolic blood pressure and PbB among males, and there was no significant association between diastolic blood pressure and PbB in either sex. Blood pressure did not change significantly between subgroups with different PbB and it seemed not to be a strong predictor of blood pressure; it was similar to some other studies in that there was only a small and weak association between PbB and blood pressure among the general population.[3 4] Also, some epidemiological studies did not find consistent results for the association between PbB and blood pressure.[10 16–18]

Several studies have, however, shown a positive association between PbB and blood pressure. Mechanisms suggested were the effect of lead on the calcium mediated control of vascular smooth muscle contraction and the renal effects mediated through the renin-angiotensin system.[2–4]

Some studies have shown an inverse correlation between body lead concentration and milk intake[19] and alcohol consumption was an effect modifier of the relation between PbB and blood pressure.[20] In this study, we considered the dietary characteristics (especially milk intake) and alcohol consumption as potential confounders for the relation between PbB and blood pressure and adjusted for these.

The relative lack of correlation in our study may be because PbB only represents the transient, and not long term, body burden of lead. Perhaps only a marker of long term body lead accumulation—such as bone lead concentration—could give a good association between blood pressure and body lead concentration.[16 17] The limitations of cross sectional study may explain the lack of association between PbB and blood pressure.

A significantly association between PbB and systolic blood pressure among males (a decrease of 10 μg/dl in PbB was associated with a decrease of 1.9 mm Hg in systolic blood pressure and 0.8 mm Hg in diastolic blood pressure) was similar to the results of other studies.[3 18] The lack of significant effects in females could be because there was only a small variation in PbB among the females in this population, which could have mitigated against finding any effects.

In summary, in this study, PbB seemed not to be a strong predictor of blood pressure, and there was only a weak association between PbB and systolic blood pressure. However, we cannot rule out a possible relation between long term body lead burden and high blood pressure.[16–18]

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